REMARKS

This is response to the non-Final Office action (Paper No. 20060505) mailed 24 May 2006.

Claims 1, 5-9, 21 and 22 are pending in this application.

Claims 1, 7-9, 21 and 22 have been amended.

I. Claim Rejections – 35 USC §102

1. Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller *et al.* ("Molecular evolution of the CMT1A-REP region: a human- and chimpanzee-specific repeat. Mol Biol Evol. 1999 Aug; 16(8): 1019-26").

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Here, the examiner failed to show that each and every element as set forth in the claim is found in Keller et al. even in view of their broadest reasonable interpretation.

(1) "said Alu element being enriched in the human genome compared to non-human primates genomes"

The feature of "said Alu element being enriched in the human genome compared to non-human primates genomes" is not found in Keller et al.

The examiner argued that Keller et al. discloses "said Alu element being enriched in the human genome compared to non-human primates genomes" in page 1023, Fig. 3c, lane hu, for example.

The examiner argued that Fig. 3c of Keller et al. shows that the amplification was observed in the human and two chimpanzee species, and not observed in, for example, gorilla and galago, and that thus, the Alu element in Keller et al. is more enriched in the human genome than non-human primates genomes.

The examiner's interpretation is not reasonable and is not consistent with the interpretation that those skilled in the art would reach.

During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). See MPEP 2111.

In view of the broadest reasonable interpretation consistent with the specification, and/or consistent with the interpretation that those skilled in the art would reach (*In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999), see MPEP 2111), the reasonable person would reach that the "compared to the non-human primates genomes" does not mean "compared to only a few specific non-human primates genomes." Also, recently the court held that the PTO should apply the principles of *Phillips v. AWH* during prosecution. ("It is well established that dictionary definitions must give way to the meaning imparted by the

specification, *Phillips v. AWH Industries*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*)" *In re Johnston*, Case No. 05-1321 (Fed. Cir. 2006).

Here, it cannot be determined that the Alu element of Keller et al. is enriched in the human genome compared to non-human primates genomes." Fig. 3c of Keller et al. does not show whether the Alu element is more enriched in the human genome than, for example, two chimpanzee species. Keller et al. did not show that there are a higher copy number of the Alu repeats in the human genome than in the non-human primates genomes.

Since each and every element is not found in Keller et al., claims 1 and 7 are not anticipated by Keller et al.

(2) "measuring the amount of the human DNA by comparing the amplified DNA with a reference"

Claims have been amended by changing "quantitating the human DNA" into "measuring the amount of the human DNA."

Since one term has been changed into another equivalent term, there is no change of the scopes of the claims, and there is no surrender of any scope of the claims.

The examiner repeatedly argued that merely comparison of the bands in an ethidium stained gel is encompassed by "quantitating the human DNA by comparing the amplified DNA with a reference." While the comparison of the band of the amplified human DNA to another band with a known amount of the human DNA may tell which has more human DNA quantity, merely comparing the human DNA band to the non-human primate DNA band does tell neither the quantity of the human DNA nor the a greater or lesser quantity of DNA than another because the human genome and the non-human genome have different copy numbers of the Alu repeats.

In other words, even if the band of the amplified human DNA is stronger than the band of the amplified non-human primate DNA, it does not necessarily mean that the quantity of the human DNA is greater than the quantity of the non-human primate DNA unless the human DNA and the non-human primate DNA have the same number of the Alu repeats.

In addition, assuming that a person gets the band which looks like the first three lanes (i.e., "hu", "pc" or "cc") in Fig. 3c from the polymerase chain reaction of an unknown sample, how can the person know whether the band is of the human DNA or of the common chimpanzee or the mixture of the human DNA and the common chimpanzee DNA?

Fig. 3c does not show even the relative quantity, but merely shows the existence of a specific band.

Withdrawal of the rejection is respectfully requested.

II. Claim Rejections – 35 USC §103

1. Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta *et al.* ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Brooks-Wilson *et al.* ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 June; 13 (2): 409-14).

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally,

the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143 - §2143.03 for decisions pertinent to each of these criteria.

The examiner failed to establish the *prima facie* case of obviousness because the above three basic criteria are not met.

(1) The prior art references when combined do not teach or suggest all the claim limitations.

First, the measurement step is neither suggested nor taught by Palmirotta et al. or in combination with Brooks-Wilson et al.

Claims 1, 21 and 22 recite "measuring the amount of the human DNA by comparing the amplified DNA with a reference." This measurement step is not found in Palmirotta et al. in view of Brooks-Wilson et al.

The examiner argued that the quantitation step is found in Figure 1 of Palmirotta et al. The Figure 1 in Palmirotta et al. merely shows that the sample is originated from primate or nonprimate. The examiner confused the mere detection of the band or the relative comparison of the bands in Palmirotta et al. or in combination with Brooks-Wilson et al. with the measurement step recited in claims 1, 21 and 22. Figure 1 itself includes only one human sample (Lane 1). From Figure 1, the quantity of human DNA (e.g., Lanes 14 and 15) cannot be measured. As stated above, even if the amplified human DNA has a stronger fluorescence band than the amplified non-human primate DNA, it does not necessarily mean that the quantity of the human

DNA is greater than the quantity of the non-human primate DNA unless the human DNA and the non-human primate DNA have the same number of the Alu repeats.

The recited references (e.g., Palmirotta et al. or in combination with Brooks-Wilson et al.) compare the amplified DNA with a reference which is related for the qualitative analysis or the comparison of the primate DNA band with the non-primate DNA band rather than the quantitation analysis of the human primate DNA. Merely comparing the amplified DNA with a reference which is not related to the human DNA cannot be equivalent to the measurement step recited in claims 1 and 7.

Furthermore, since the purpose of Palmirotta et al. is to determine the origin and gender of dried blood on a statue of the Virgin Mary, there is no suggestion or teaching to perform the measurement step in Palmirotta et al. or in combination with Brooks-Wilson et al. Also, there is no desirability of adding the measurement step.

Therefore, claims 1 and 7 are not obvious over Palmirotta et al. in view of Brooks-Wilson et al.

Second, the intra-Alu PCR is neither suggested nor taught by Palmirotta et al. or in combination with Brooks-Wilson et al.

The examiner argued that "Brooks-Wilson et al. teaches a method of intra-Alu PCR (i.e., Alu element mediated PCR) for amplification of human sequences."

However, the Alu-PCR system in Brooks-Wilson et al. is not "intra Alu PCR". Brooks-Wilson et al. discloses that "we synthesize only those sequences found between Alu elements that are in opposite orientations and within a distance appropriate for PCR amplification" (see page 614, col. 2, first paragraph) and "The use of a primer from the extreme 3'end of the Alu

repeat allows us to synthesize DNA molecules that are largely free of Alu-derived repeat sequences. The observation... that few of them contain repetitive DNA, may be a reflection of the general nature of inter-Alu sequences." (See page 618, second paragraph.)

Accordingly, the Alu-PCR system in Brooks-Wilson et al. is not "intra Alu PCR".

Since the examiner failed to establish a *prima facie* case of obviousness, withdrawal of the rejection is respectfully requested.

Therefore, claims 1 and 7 are patentable, and their dependent claims 2-3, and 5-9 are also patentable.

(2) The examiner failed to show the feature of "said Alu element being enriched in the human genome compared to non-human primates genomes."

The examiner argued that this feature is shown in Figure 1, lanes 1 and 9-15 of Palmirotta et al. However, Lanes 9-15 of Figure 1 are not for non-human primates, but for mouse, ox, pig, etc. Palmirotta et al. expressly admitted that from Figure 1 it can be concluded that the statue blood originated from humans or from a non-human catarrhine primate. (See page 432, second column last three lines and page 433,, first column, first two lines). That is, from figure 1, it cannot be determined whether the statue blood originated from humans or from a non-human catarrhine primate. Brooks-Wilson et al. does not teach this feature, either. In Brooks-Wilson et al., the Alu PCR is used to distinguish the human material from the rodent DNA.

In response to the applicant's arguments, the examiner further argued that "while Alu PCR product was obtained from human samples, no Alu PCR was obtained in New World monkey Saimiri sciurerus. The above feature recited in Claim 1 does not require that the Alu element being absent from every non-human primate genome."

It is true that claim 1 does not require that the Alu element being absent from every non-human primate genome, but claim 1 does require that Alu element is enriched in the human genome compared to non-human primate genomes. In view of the broadest reasonable interpretation consistent with the specification, and/or consistent with the interpretation that those skilled in the art would reach (*In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999), see MPEP 2111), the reasonable person would reach that the "compared to the non-human primates genomes" does not mean "compared to a few specific non-human primates genomes." The examiner's interpretation is not reasonable interpretation consistent with the specification, and/or consistent with the interpretation that those skilled in the art would reach. Also, recently the court held that the PTO should apply the principles of *Phillips v. AWH* during prosecution. ("It is well established that dictionary definitions must give way to the meaning imparted by the specification, *Phillips v. AWH Industries*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*)" *In re Johnston*, Case No. 05-1321 (Fed. Cir. 2006).

Since the feature of "said Alu element being enriched in the human genome compared to non-human primate genomes" is not found in the references, claims 1 and 7 and their dependent claims are patentable.

2. Claims 1, 7, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll *et al.* ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Brooks-Wilson *et al.* ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 June; 13(2): 409-14).

(1) The prior art references when combined do not teach or suggest all the claim limitations.

First, the measurement step is neither suggested nor taught by Carroll et al, or in combination with Brooks-Wilson et al.

Claims 1, 7, 21 and 22 recite "measuring the amount of the human DNA by comparing the amplified DNA with a reference." The measurement step is not found in Carroll et al. even in view of Brooks-Wilson et al.

The examiner argued that the measurement step is found in page 38, col. 2, paragraph 1 of Carroll et al. However, Carroll et al. merely discloses that PCR products can be directly visualized using UV fluorescence. This is not a quantitation step, but a qualitative assay step. The purpose of Carroll et al. is to analyze human genome diversity. There is no suggestion or teaching to perform the quantitation step in Carroll et al. The examiner confused the possibility of quantitation with the actual quantitation step.

The recited references (e.g., Carroll et al. or in combination with Brooks-Wilson et al.) compare the amplified DNA with a reference which is related for the qualitative analysis or the comparison of the primate DNA band with the non-primate DNA band rather than the quantitation analysis of the human primate DNA. Merely comparing the amplified DNA with a reference which is <u>not</u> related to the human primate DNA cannot be equivalent to the measurement step recited in claims 1, 7, 21 and 22.

Therefore, withdrawal of the rejections of claims 1, 7, 21 and 22 and their dependent claims is respectfully requested.

Second, the intra-Alu PCR is neither suggested nor taught by Carroll et al. or in combination with Brooks-Wilson et al.

The examiner argued that "Brooks-Wilson et al. teaches a method of intra-Alu PCR (i.e., Alu element mediated PCR) for amplification of human sequences."

However, the Alu-PCR system in Brooks-Wilson et al. is not "intra Alu PCR". Brooks-Wilson et al. discloses that "we synthesize only those sequences found between Alu elements that are in opposite orientations and within a distance appropriate for PCR amplification" (see page 614, col. 2, first paragraph) and "The use of a primer from the extreme 3'end of the Alu repeat allows us to synthesize DNA molecules that are largely free of Alu-derived repeat sequences. The observation... that few of them contain repetitive DNA, may be a reflection of the general nature of inter-Alu sequences." (See page 618, second paragraph.)

Accordingly, the Alu-PCR system in Brooks-Wilson et al. is not "intra Alu PCR".

Since the examiner failed to establish a *prima facie* case of obviousness, withdrawal of the rejection is respectfully requested.

Therefore, claims 1, 7, 21 and 22 are patentable, and their dependent claims 2-3, and 5-9 are also patentable.

(2) Carroll et al. in view of Brooks-Wilson et al., does not teach or suggest the present invention.

Please note that the corresponding author of Carroll et al. is Dr. Batzer, who is one of the inventors of the present invention.

The fact that the specific sequences are found as a 100% match within a theoretical consensus (or average) sequence of primate mobile elements (Alu) in general (about 300 bp) in

no way suggests the knowledge or intention of having any clue about actually isolating these particular short sequences for 1) use as PCR primers; 2) Intra-Alu PCR amplification from young human specific elements (in contrast to the theoretical concept of Alu elements in general common to all primate species or limited subsets of species); 3) for quantitation (not just detection) of human DNA.

For the foregoing reasons, withdrawal of the rejections of claims 1, 7, 21 and 22 and its dependent claims is respectfully requested.

3. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll *et al.* ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Brooks-Wilson *et al.* ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 June; 13(2): 409-14), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats' Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252) and Buck *et al.* ("Design Strategies and Performance of Custom DNA Sequencing Primers") BioTechniques. September 1999. 27: Pages 528-536).

Claim 5 depends from claim 1. The applicant explained why claim 1 is patentable. Accordingly, claim 5 is also patentable.

In addition to the arguments above for claim 1, the examiner failed to establish a *prima facie* case of obviousness for the following additional reasons.

Jurka merely discloses the comparison of Alu Sb1 subfamily consensus sequence with Alu Sb2 family consensus sequence, but does not disclose the specific primers. It is hardly

understood how the ordinary skilled person can use the claimed sequences in view of Jurka and/or in combination with the other references. The examiner's reasoning is that, if the human genome sequences are known, all the primers based on that sequence are also obvious. This reasoning cannot be acceptable. There is no desirability of using the claimed sequences on the basis of the prior art references.

As stated above, the fact that the specific sequences are found as a 100% match within a theoretical consensus (or average) sequence of primate mobile elements (Alu) in general (about 300 bp) or small groupings or subfamilies of the elements in no way suggests the knowledge or intention of having any clue about actually isolating these particular short sequences for 1) use to design PCR primers; 2) Intra-Alu PCR amplification from young human specific elements (in contrast to the theoretical concept of Alu elements in general common to all or some primate species); 3) for quantitation (not just detection) of human DNA.

It should be also noted that the examiner cited *In re Deuel*, 34 USPQ2d 1210 (Fed. Cir. 1995), by stating that "the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does **not** make the specific DNA **obvious**." (emphasis added.) This holding clearly shows that the examiner's rejection is not proper.

The examiner also argued that "Buck expressly provides evidence of the equivalence of primers."

As cited by the examiner, the Court of Appeals for the Federal Circuit held that the existence of a general method of gene cloning in the prior art is not sufficient, without more, to render obvious a particular cDNA molecule. *In re Deuel*, 34 USPQ2d 1210 (Fed. Cir. 1995). In *In re Deuel*, the court stated that "even if, as the examiner stated, the existence of general cloning techniques, coupled with knowledge of a protein's structure, might have provided motivation to

prepare a cDNA or made it obvious to prepare a cDNA, that does not necessarily make obvious a particular claimed cDNA. "Obvious to try" has long been held not to constitute obviousness. In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." 34 USPQ2d at 1216. The court also stated that "a conceived method of preparing some undefined DNA does not define it with the precision necessary to render it obvious." *Id.*

The applicant respectfully requests the examiner to explain how the holding of *In re Deuel* is distinguished from the present case.

Since the examiner failed to establish a *prima facie* case of obviousness, withdrawal of the rejection is respectfully requested.

4. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta *et al.* ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Brooks-Wilson *et al.* ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 June; 13 (2): 409-14), in view of Gelmini *et al.* ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Claims 8 and 9 depend from claim 1. The applicant explained why claim 1 is patentable. Accordingly, claims 8 and 9 are also patentable.

In addition to the arguments above for claim 1, the examiner failed to establish a *prima facie* case of obviousness for the following additional reasons.

Additionally, there is no suggestion or motivation to combine reference teachings.

The purpose of Palmirotta et al. is to determine the origin and gender of dried blood on a statue of the Virgin Mary, and the purpose of the Alu PCR in Brooks-Wilson et al. is to clone and map human DNA markers. Since the purposes of the above references are not related to the measurement of the amount of the human DNA, there is no reason to perform the measurement step in view of Gelmini et al.

The examiner merely argued the advantages of using fluorogenic probes in quantitative polymerase chain reaction-based homogeneous assay is a motivation to combine the references, but did not provide why the measurement of the amount of the human DNA should be used or desirable in Palmirotta et al., and/or Brooks-Wilson et al.

Since the examiner failed to establish a *prima facie* case of obviousness,

Therefore, claim 8 and 9 are patentable.

5. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll *et al.* ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Brooks-Wilson *et al.* ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 June; 13 (2): 409-14), in view of Gelmini *et al.* ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Claims 8 and 9 depend from claim 1. The applicant explained why claim 1 is patentable. Accordingly, claims 8 and 9 are also patentable.

In addition to the arguments above for claim 1, the examiner failed to establish a *prima facie* case of obviousness for the following additional reasons.

Additionally, there is no suggestion or motivation to combine reference teachings.

The purpose of Carroll et al. is to determine the human genomic diversity based upon locus specific insertion presence or absence, and the purpose of the Alu PCR in Brooks-Wilson et al. is to clone and map human DNA markers. Since the purposes of the above references are not related to the measurement of the amount of the human DNA, there is no reason to perform the measurement step in view of Gelmini et al.

The examiner merely argued the advantages of using fluorogenic probes in quantitative polymerase chain reaction-based homogeneous assay is a motivation to combine the references, but did not provide why the measurement of the amount of the human DNA should be used or desirable in Palmirotta et al., and/or Brooks-Wilson et al.

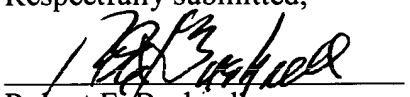
Since the examiner failed to establish a *prima facie* case of obviousness,

Therefore, claim 8 and 9 are patentable.

No fees are incurred by this Amendment.

In view of the above, all claims are submitted to be allowable and this application is believed to be in condition to be passed to issue. Reconsideration of the rejections is requested. Should any questions remain unresolved, the Examiner is requested to telephone Applicant's attorney.

Respectfully submitted,



Robert E. Bushnell
Attorney for the Applicant
Registration No.: 27,774

1522 "K" Street N.W., Suite 300
Washington, D.C. 20005
Tel. No. (202) 408-9040
Facsimile No. (202) 289-7100

Folio: P56885
Date: 8/16/2006
I.D.: REB/JHP